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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/629,975	07/30/2003	James Hunter Boone	TLAB.79219	9513

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EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/629,975	BOONE ET AL.	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

– The MAILING DATE of this communication appears on the cover sheet with the correspondence address –

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicants response to the Office Action mailed 16 November 2005 is acknowledged (paper filed 5/26/06). In the amendment filed therein claims 1, 3, and 6 were modified. Currently claims 1-6 are pending and under consideration.

2. Rejections and/or objections of record not reiterated herein are withdrawn.

NEW GROUNDS OF REJECTION NECESSITATED BY AMENDMENT

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-2 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1 is vague and indefinite because the comparison step is directed to monitoring inflammatory bowel disease in a patient but the preamble merely measures the concentration of total lactoferrin. Therefore it is not clear as to what the method encompasses. The method lacks a resolution step, which reads back on the preamble of claim 1. Please correct.

B. In claim 1, the comparison step is vague and indefinite because it recites "the patient" and "treatment". However, these claims lacks antecedent basis in the claim. In particular, a patient sample is not specifically measured nor is a treatment required by the claim. In order to obviate the rejection it is suggested that the claim contain consistent language that clearly sets forth the process intended. Appropriate correction is required.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 3-5 (Claim 3 and its dependent claims 4-5) are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 3 recites the limitation of "calculated lactoferrin equal to or greater than 7.25μg/ml. However, the specification does not provide support for this range. Specifically, the 7.25μg/ml value is not taught. On page 35 section 0062, two lactoferrin concentrations are taught 9749.37μg/mL in active disease patients and 7.42μg/mL with patients in remission. The 7.25μg/mL value is not discussed. Applicant is invited to show support for the 7.25μg/mL value recited in claim 3.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

I. Claim 6 is rejected under 35 U.S.C. 102(e) as being anticipated by Hayes et al. (US Patent #6,358,939 B1).

Hayes et al. disclose methods for treating inflammatory bowel disease (IBD) with biologically active vitamin D compounds. See abstract and column 4 lines 41-67, for example. In order to assess/monitor the disease and treatment results, fecal lactoferrin concentrations are measured. See column 20 lines 50-51 and lines 60-61, for example. The assay for lactoferrin employs a two-site ELISA wherein the samples are measured from the linear portion of a log-linear plot at A-450nm. See column 21 lines 36-52. Lactoferrin is measured at two-day interval (first fecal sample at a first time). See column 23 lines 46-47. Calcitriol is begun when the mice are suffering from IBD (treatment). See column 23 lines 47-48. Thereafter, stool samples are obtained at four-day intervals until the mice were euthanized on day 22 (second fecal sample). See column 23 lines 50-54. The results indicated that calcitrol treatment of mice exhibiting symptoms of IBD were reduced as compared to controls. See column 23 lines 58-61. this method is also taught to be useful in monitoring humans with IBD see column 23 line 65 to column 24 line 19.

Response to Arguments

Applicant's arguments and amendment to claim 6 was found persuasive. Because Sugi et al. did not teach measurements of lactoferrin as a means for monitoring IBD treatment, it was replaced with US patent #6,358,939 to Hayes et al.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

II. Claims 1-2 are rejected under 35 U.S.C.103(a) as being unpatentable over Hayes et al. (US Patent #6,358,939 B1) in view of Uchida et al. (US Patent #5,552,292).

Please see Hayes et al. as set forth above.

Hayes et al. differ from the instant invention in not specifically teaching fecal sample dilution procedures.

However, Uchida et al. teach methods to measure lactoferrin in fecal samples. Lactoferrin is taught to be a marker for various diseases related to inflammatory gastrointestinal disorders and colon cancer. Column 2 lines 46-59. Lactoferrin was found to be the most stable substance in feces. Column 3 lines 10-11. Specifically a polyclonal antibody for lactoferrin (DAKOPATT) is employed to measure lactoferrin in inflammatory diarrhea specimens. Column 5 lines 57-61.

The method was performed in an enzyme-linked immunoassay format. A polyclonal antibody against lactoferrin (anti-human lactoferrin antibody) is immobilized onto wells of a 96-well polystyrene micro plate. The plate is contacted with diluted fecal specimen (column 11 lines 31-33 wherein 50Tl of sample is added to 100Tl %1BSA and TBS buffer) and detected with a polyclonal antibody labeled with alkaline phosphatase (anti-human-lactoferrin antibody). See column 11 example 2 and column 5 lines 14-19. The results were correlated to standards prepared with purified lactoferrin. Column 6 lines 13-19.

The assay results were detected at 510/630nm absorbance. Column 11 lines 53-56. Increased levels of lactoferrin were demonstrated to several diseases. See column 12-Results.

Uchida et al. disclose standard curve comparative analyses (claim 2). Healthy person fecal samples were run and graphed on a curve for comparison to unknown sample sets (standard curve). Column 7 lines 51-64 and column 8 lines 18-29.

Kit embodiments are also disclosed. The kit contains antibodies immobilized on a solid phase (micro plate), an enzyme linked antibody, and a chromogene (enzyme substrate for color development). See column 4 lines 1-9 and column 5 lines 36-40.

With respect to endogenous lactoferrin, it is noted that the lactoferrin detected by Uchida et al. were found within the patient (endogenous to the patient) and occurred as a result of disorders.

Normal patients exhibited very small amounts of lactoferrin (0.75 – 2.4Tg/g feces) and Uchida et al. taught that their method could be used in various types of lactoferrin (column 6 lines 58-61). Therefore absent evidence to the contrary Uchida et al. teach the detection of endogenous lactoferrin.

Uchida et al. taught that sample dilution was useful in ensuring that the sample concentrations could be compared to LF quantification curve for accurate measurements with in the assay range. See column 11 lines 56-63.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to dilute lactoferrin fecal samples as taught by Uchida in the lactoferrin assay of Hayes et al. because Uchida et al. taught that sample dilution was useful in ensuring that the sample concentrations could be compared to LF quantification curve for accurate measurements with in the assay range. See column 11 lines 56-63. Absent evidence to the contrary the dilution of the lactoferrin sample as taught by Uchida et al. is routine optimization.

It would have been obvious to one having ordinary skill in the art at the time of the invention was made to dilute lactoferrin, since it has been held that discovering an optimal value of a result effective variable involves only routine skill in the art. In re Boesch, 617 F.2d 272, 205, USPQ 215(CCPA 1980).

Response to Arguments

Applicant contends that Uchida does not teach fecal sample dilution. This argument was carefully considered but not found persuasive because Uchida teaches procedures involving a fecal sample that is mixed with TBS buffer (diluted with TBS) and applied to an immunoassay. See column 5 lines 11-13 and column 11 lines 12-15, for example.

Applicant argues that the reference to Boy Hoeyer teaches linear calibration for quantitative chemical analysis but is not related to biological markers. This argument was carefully considered and found persuasive. US Patent #6,358,939 to Hayes et al. has been added to the rejection. Hayes et al. taught that their assay for lactoferrin employs a two-site ELISA wherein the samples are measured from the linear portion of a log-linear plot at A-450nm. See column 21 lines 36-52.

III. Claims 3-5 are rejected under 35 U.S.C.103(a) as being unpatentable over Uchida et al. (US Patent #5,552,292) in view Foster et al. (U.S. Patent#4,444,879).

Please see Uchida et al. as set forth above. Further, Uchida et al. disclose that lactoferrin concentrations in fecal samples were obtained from a lactoferrin quantification curve.

The assay range was 10.0 to 1000.0 ng/ml (10,000 to 1,000,000μg/ml). See column 11 lines 56-67. This read on Applicants measurements of lactoferrin at levels equal to or greater than 7.25μg/ml.

Although Uchida et al. teach the regents required by the claims, they do not specifically teach the inclusion of all the reagents in kit configurations (in particularly the purified human lactoferrin – taught in '292 column in column 6 lines 14-16 and stop solution or coloring reagent – taught in '292 column 5 line 29-30). In other words, the reference fails to teach all the reagents as a kit. However, kits are well known embodiments for assay reagents. Foster et al. (U.S. Patent #4,444,879) describe one example.

In their patent kits including the reactant reagents, a micro plate, positive controls, negative controls, standards, and instructions are taught. The reagents are compartmentalized or packaged separately for utility. See figure 6, and column 15, lines 10-34.

It would have been prima facie obvious to one of ordinary skill in the art at the time of applicant's invention to take the detection assay reagents as taught by Uchida et al. and format them into a kit because Foster et al. teach that it is convenient to do so and one can enhance sensitivity of a method by providing reagents as a kit. Further, the reagents in a kit are available in pre-measured amounts, which eliminates the variability that can occur when performing the assay. Kits are also economically beneficial in reagent distribution.

It is also worth noting that the printed matter on instructions merely teaches the use of an existing product, and thus cannot impart patentability. See *In re Ngai*, 5/13/04, Michel, Gajarsa, Linn, per curiam. In other words the printed matter on the instructions in a kit cannot serve to define the kit over the prior art. See *In re Gulack,* 217 USPQ (CAFC 1983).

Response to Arguments

Applicant contends that the Uchida reference fails to teach or suggest all the limitations of the rejected claims.

Applicant argues that Uchida et al. discloses methods for diagnosing gastrointestinal tract disorders, particularly colorectal cancer. This argument was carefully considered but not found persuasive because Uchida et al. teach methods to detect IBDs like ulcerative colitis and Cohn's disease. See table 2 and column 3 lines 20-39, for example.

Specifically applicant argues that Uchida measures the level of only whole-sized lactoferrin by immunoassay utilizing monoclonal antibodies. This argument was carefully considered but not found persuasive because Uchida discloses the detection of total lactoferrin (whole and half-sized) with a polyclonal antibody.

Lactoferrin was measured by immunoassay utilizing polyclonal antibody (DAKOPATT, Denmark, referred to as DAKO). The results showed two types of lactoferrin; whole and half-sized. See column 5 lines 57 through column 6 line 2.

Further, the test for obviousness is not whether the features of one reference may be bodily incorporated into the other to produce the claimed subject matter but simply what the combination of references makes obvious to one of ordinary skill in the pertinent art. See, *In re Bent,* 52 CCPA 850, 144 USPQ.28 (1964); *In re Nievelt,* 179 USPQ 224 (CCPA 1973).

Applicant's arguments with respect to the measurement of lactoferrin against a standard curve have been considered but are not persuasive because Uchida teaches this limitation in column 11 line 64-66 for example.

The newly added limitations regarding the determination of lactoferrin at a value equal to or greater than 7.25μg/ml is taught by Uchida et al. Specifically, Uchida et al. taught that the assay range was 10.0 to 1000.0 ng/ml (10,000 to 1,000,000μg/ml). See column 11 lines 56-67.

Applicant contends that the rejections under 103(a) including Foster 4,444,879 should be withdrawn because of the deficiencies noted in Uchida et al. The deficiencies in Uchida et al. have been addressed above. Accordingly, the rejections are maintained.

7. For reasons aforementioned, no claims are allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group TC 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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